

"How to Prepare Your First Grant Application: A Survival Guide"

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Talk outline:

- **Pre-submission: Deciding what to include and when to prepare your first RO1 application.**
 - Develop an idea.
 - Guidelines for reviewers.
 - Familiarize with all the required sections of the grant.
- How much preliminary data do I need?
- How much time do I need to prepare the application?
- Selecting a study section.

Talk outline:

- **Post-submission**

- Can I submit additional data after submission?
- Interpreting your score and responding to comments by the reviewers.
 - What if my application is not scored?
 - Should I change study sections?

Basic ingredients of a grant application

Novel idea



**Good
writing/presentation
style**



**Good
experimental
approach**



Collecting preliminary results

- Start early: a minimum of 2-3 months before the deadline
- Be technically innovative, use state-of-the approaches
- Focus on your strengths.
- Collaborate, if necessary, but avoid the appearance of lack of intellectual independence.

Know how your application will be evaluated

Innovation

- Conceptual
- Technical

Investigator

- Expertise
- Productivity
- Independence

Significance

Environment

- Intellectual
- Available
instrumentation, etc.

Approach

- Focus
- Likely to generate conclusive data
- Sound experimental approach
- State-of-the art techniques

How does everything start?



Development of a novel idea

- Discovery of novel protein, process, technique, etc.

QuickTime™ and a
Video decompressor
are needed to see this picture.

- Novel approach to solve a controversial issue

Familiarize yourself with the PHS398 application forms and instructions

- Face page
- Abstract 
- Personnel
- Modular budget/Budget justification
- Resources
- Research plan
 - Specific aims 
 - Background and significance
 - Preliminary results
 - Research design and methods

Tips for an effective abstract

- **Abstract**

Tip 1: visit <http://crisp.cit.nih.gov/> and study the abstracts of several funded grants



Tip 2: Make sure your abstract includes the following:
Background (e.g. highlight any controversy in the field), **overall goal of the grant** (big picture), **summary of preliminary data, aims, techniques and significance.**

An example of an effective abstract

(taken from 2R01HL036974-18, W.J. Lederer P.I.)

The elementary unit of Ca^{2+} release in heart muscle is the calcium spark... The molecular mechanisms that underlie...remain **elusive or controversial**. The proposed work will use **new methods developed by the PI** ... **resolve the conflicts**...**Preliminary results suggest** that all proposed experiments can be done and should provide important new information. **There are four questions that the proposed work seeks to address**. 1. How does the triggering of Ca^{2+} sparks depend on $[\text{Ca}^{2+}]_i$ and important cellular regulators of EC coupling?...The **planned work will provide fundamental**...how molecular and cellular alterations of such signaling systems lead to specific pathologies and novel treatments.

Tips for an effective Specific Aims section

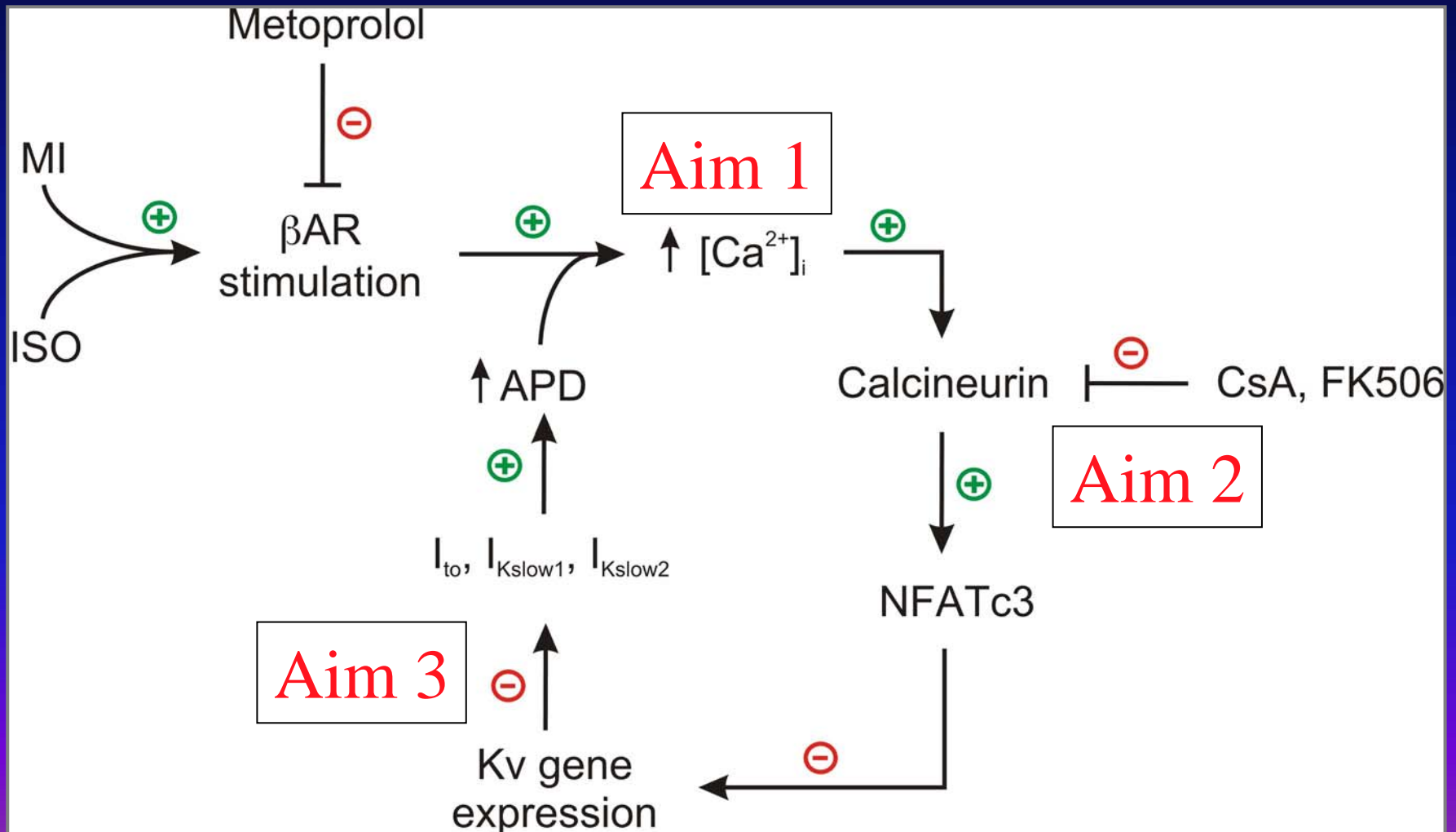
- **Background (introductory paragraph)**
 - Overall goal (big picture)
 - Put your area of research in perspective
- **Summary of preliminary results**

- **Clearly state the aims of your grant and how you will test them**

Specific Aim 2: To test the hypothesis that reduced expression of the $\beta 1$ subunit of BK channels during hypertension reduces the sensitivity of these channels to physiological changes in Ca^{2+} .

This aim has three experimental series. The first experimental series will test the hypothesis that expression of the $\beta 1$ subunit of BK channels decreases in cerebral vascular smooth muscle as blood pressure increases...

- Use a cartoon of the explain the issues addressed by the proposal



Background and significance

- Do not write it as a review article
- Highlight controversies and how they will be solved by the proposed experiments
- Link controversies and outstanding issues to relevant sections in your grant

Example

“... permanent ablation of genes could lead to **compensatory, or even maladaptive**, changes in the expression of other genes. Thus, one must wonder if $\beta 1$ down-regulation is the only cause for the electrophysiological changes seen in $\beta 1$ knock out smooth muscle. Indeed, **an important question not addressed by** ...is what happens to Kv currents in $\beta 1$ knock out vascular smooth muscle. Are Kv currents reduced in $\beta 1$ knock out smooth muscle? **The experiments outlined in this application will examine this specific issue.**”

Preliminary Results

- How much preliminary data do I need?
- Prepare effective graphs

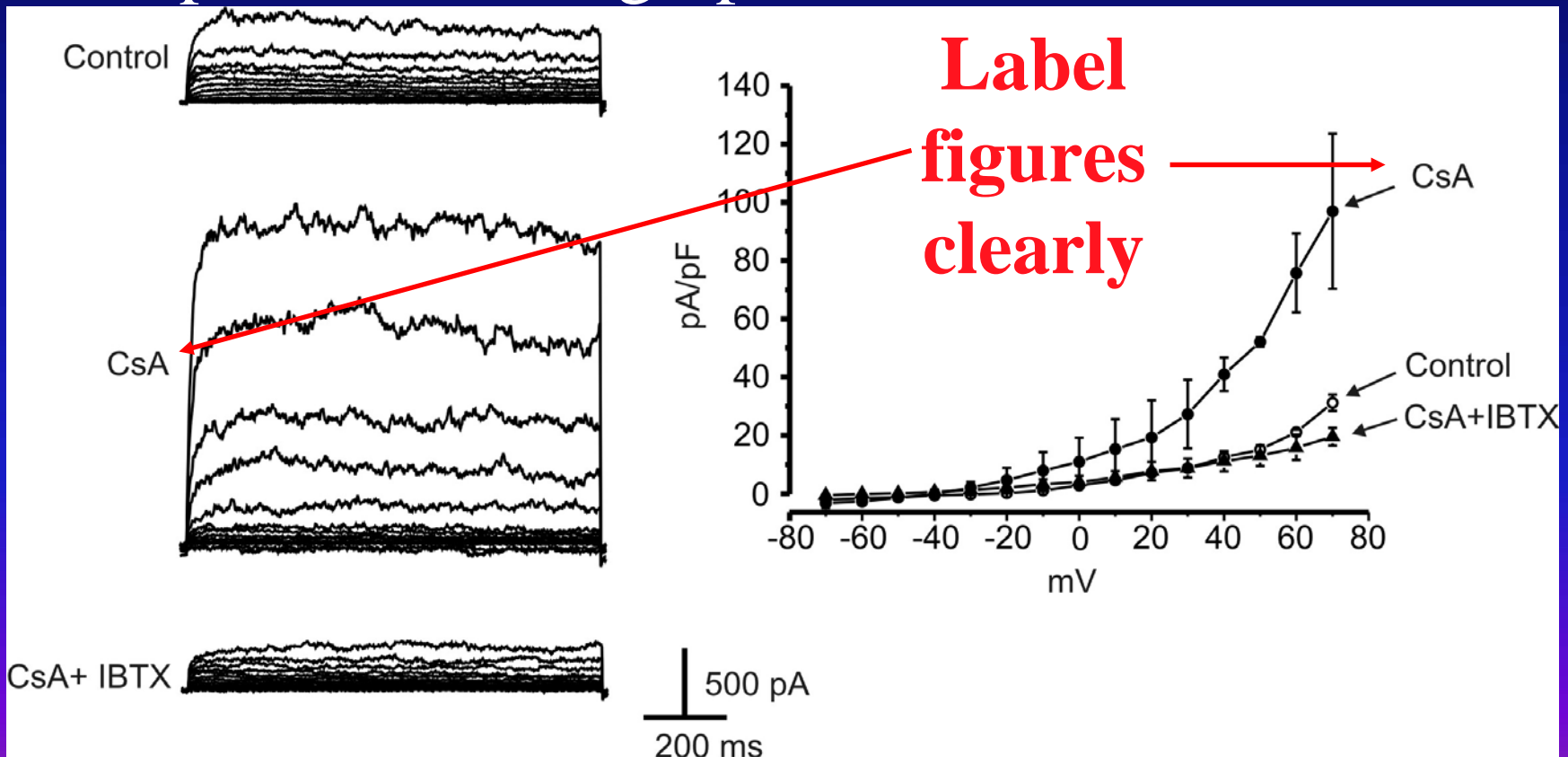


Fig. 4... (Santana et al. unpublished results)

Research Design

Aim

- Rational: Why are these experiments important?
- Sub-aims (hypotheses)
 - Specific experiments
 - Expected results

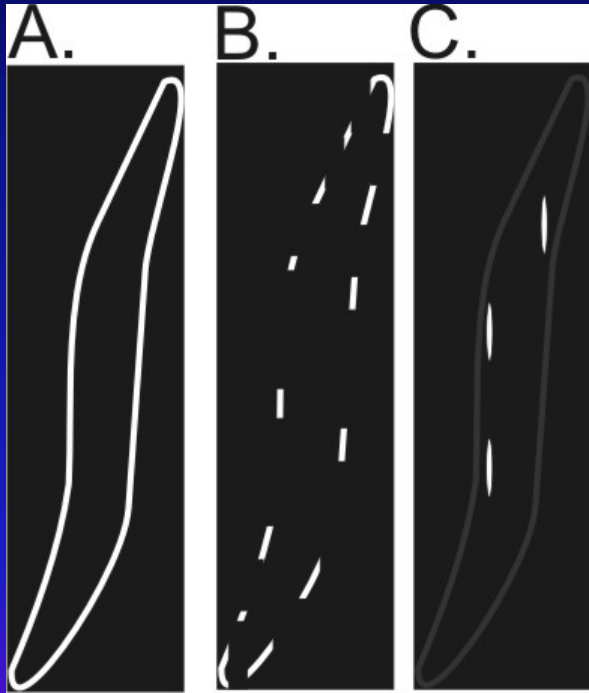
Specific Aim 1: To test the hypothesis...

Rationale: Our preliminary results suggest that calcineurin regulates BK channel function in VSM. The experiments outlined below will investigate the mechanisms and functional consequences of BK channel modulation by acute activation of calcineurin in ...

Experimental series 1.1 will test the hypothesis that calcineurin opposes the actions of PKA on BK channels.

Specific experiments. Testing this hypothesis involves recording macroscopic BK channel currents using the whole-cell configuration of the patch-clamp technique.

Expected results



Case 1

Case 3

Case 2

- Use cartoons
- Consider all possible experimental outcomes
- What would you conclude in the different scenarios?
- Refer to preliminary results when a specific outcome is expected

Consult with your colleagues

About a month before the grant is due ask 2-3 colleagues to read your grant and offer feedback

- 2 experts
- 1 scientist in an unrelated field

Submitting your application

Prepare a cover letter requesting a study section and institute(s)

http://www.csr.nih.gov/Roster_proto/sectionI.asp

- **Relevant expertise**
- **Look for sympathetic, fair reviewers**

After the application has been assigned:

- **Contact your SRA and ask about submitting supplementary material**

Interpreting the results of the review process

- What if my application is not scored?
 - Wait for the comments by the reviewers.
 - Rewrite
 - Rewrite and submit to different study section

Easy to respond to:

“It is not clear why permeabilization of the cells outside the patched area was not proposed.”

Excellent suggestion. We have now incorporated these experiments into our proposal.

Not so easy to respond to:

“The research plan is overambitious”

